

## The dynamics of microRNA in aging: Embrace, trace and ace

Akbar Shoukat Ali

Madam, aging is regarded as a complex, controlled and synchronized process that constitutes a mass of unfavorable adjustments which progressively deteriorates the cellular and molecular pathways sustaining life; leading to cessation of vital physiological processes and ultimate death.<sup>1</sup> The never-seen-before advancements in molecular sciences have empowered the tracing of 'molecular players' leading towards aging. One such novel player within the domain of aging is the microRNA. MicroRNAs are single stranded, bi-polar (18-25 nucleotides in length), non-protein-coding RNAs that negatively operate the process of gene expression by modifying post-transcriptional targets on messenger RNA.<sup>2</sup> They embrace 1-5% of the human genome.<sup>3</sup>

Harries (2014) has comprehensively reviewed the role of microRNA, affecting the nine major determinants of aging; 1) Genomic Alterations: Our genome has highly conserved DNA maintenance mechanisms which preserve the integrity of DNA from exogenous and endogenous insults. Such a key role is played by microRNAs especially microRNA-192, microRNA-194 and microRNA-215 by molecular arrest of DNA replicative cycle; 2) Shortening of Telomeres: Similarly, microRNAs such as microRNA-34, microRNA-138 and microRNA-155 are linked with maintenance of telomere length; to avoid premature 'telomere crisis' and aging; 3) Epigenetic Regulation: A cocktail of microRNAs have also been associated with epigenetic regulation of aging; by histone modification (microRNA-15a, microRNA-16 and microRNA-29) and splicing (microRNA-519, microRNA-16 and microRNA-125a); 4) Proteostasis: Deregulation of protein homeostasis leads to abnormal protein aggregation within cell. A network of proteins called 'Chaperone', which is related to aging, has been found to be regulated by microRNAs (microRNA-1, microRNA-26b, microRNA-106a and microRNA-301b and microRNA-320); 5) Dysfunctional Nutrient Sensing: Likewise, microRNA-1, microRNA-17, microRNA-19b, microRNA-20a, microRNA-106a, microRNA-126, microRNA-190b, microRNA-206 and miR-320 have been associated with abnormal nutrient sensing by cells and aging thereafter; 6) Mitochondrial impairment: Mitochondria

is vulnerable to damage by reactive oxygen species (ROS). The enzymes that prevent mitochondria from ROS injury are also regulated by microRNAs (microRNA-335 and microRNA-34a); 7) Cellular deterioration: MicroRNAs that regulate genomic alteration and telomere shortening have been implicated in cellular deterioration as well, as it is the consequence of former cellular events; 8) Stem cell depletion: Several microRNAs, especially microRNA-29c, microRNA-371, microRNA-369-5p, microRNA-499 have been proved to impede stem cell potency; and 9) Inflammation: Evidence suggests that few microRNAs, so-called 'inflammamicroRNA' are proactive in aging, microRNA-21, microRNA-146a and microRNA-155 in particular. These microRNAs have also been shown to regulate chronic diseases such as cardiovascular disease, Alzheimer's disease and rheumatoid arthritis.<sup>4</sup>

Given the rising trend of aging population in Pakistan, as suggested by Jalal et al.,<sup>5</sup> it is plausible that insight into the entirety of microRNA in modulating aging holds great promise; however, scientific literature is yet to emanate from Pakistan. Intriguingly, it would be worth investigating the molecular dynamics of microRNA in Pakistani population and how best it correlates with aging and age associated chronic diseases and, certainly, will be succoring as a guiding principle for devising diagnostic and therapeutic interventions accordingly.

**Disclaimer:** None

**Conflict of Interest:** None

**Sources of Funding:** None

### References

1. Huan T, Chen G, Liu C, Bhattacharya A, Rong J, Chen BH, et al. Age-associated microRNA expression in human peripheral blood is associated with all-cause mortality and age-related traits. *Aging Cell*. 2018; 17: 12-8.
2. Jung HJ, Suh Y. MicroRNA in Aging: From Discovery to Biology. *Current genomics*. 2012; 13:548-57.
3. Hoareau-Aveilla C, Meggetto F. Crosstalk between microRNA and DNA Methylation Offers Potential Biomarkers and Targeted Therapies in ALK-Positive Lymphomas. *Cancers (Basel)*. 2017; 9: 22-41.
4. Harries LW. MicroRNAs as Mediators of the Ageing Process. *Genes*. 2014; 5:656-70.
5. Jalal S, Younis MZ. Aging and Elderly in Pakistan. *Ageing Inter*. 2014; 39:4-12.

.....  
Aga Khan University Hospital, Karachi.

**Correspondence:** Akbar Shoukat Ali. Email: akber.shoukat.ali@gmail.com